CRITERIA for IMMUNE RESPONSE MODIFIER PATHWAY PRIORITIZATION

The following has been recommended as criteria to assess Translational Research Opportunities in the Immune Response Modifier Pathway.

The criteria categories are indicated in the colored bars, and correspond to domains within the TRWG Immune Response Modifier Pathway (Clinical Cancer Research 14: 5692-5699, 2008) (http://clincancerres.aacrjournals.org/content/vol14/issue18/#CCR_SPECIAL_FOCUS). Subcriteria are indicated for each criteria, and correspond to information available on the scientific validity and feasibility of accelerating the development of the Opportunity to the point of early stage clinical trials. Rating scales and corresponding definitions indicate the level of evidence available for each subcriteria in descending order of robustness.

Opportunities demonstrating a high level of scientific validity and feasibility using these criteria will be further assessed by the NCI for clinical need and appropriateness for NCI investment. The resulting information will used in a variety of ways by the NCI, including but not limited to: 1) to inform the development of RFPs, RFAs, PAs, CRADAs, and/or Cooperative Agreements, including a limited number of Special Translational Research Acceleration Projects (STRAPs) through the NCI's Process to Accelerate Translational Science Initiative, 2) to inform the development, formulation, production and implementation of products/devices/processes through internal NCI mechanisms, or 3) no action taken. The information is designed to assist the NCI in facilitating the advancement of promising translational research Opportunities through the developmental process as rapidly, effectively, and efficiently as possible.

Creation of Modality and Development Domains of the Immune Response Modifier Pathway

CRITERIA Subcriteria	RATING SCALE	LEVEL OF EVIDENCE in descending order
ANTIGEN		
Immunogenicity	T cell and/or antibody responses elicited to antigen in clinical trials	Data supports this antigen as being immunogenic in clinical trials
	Spontaneous T cell responses to antigen observed in some patients	Data supports T cell immunity observed in some patients
	Immunogenic in animal models with natural levels of antigen expression similar to humans	Data supports this antigen as being immunogenic in appropriate animal models
	Spontaneous antibodies to antigen observed in some patients	Antibodies to this antigen are observed in some patients
	No data available	No data available

Therapeutic function	Efficacy in a controlled vaccine clinical trial	Data that antigen elicits a therapeutic response in a controlled vaccine trial is extremely convincing as judged by an informed expert
		Data that antigen elicits a therapeutic response in a controlled vaccine trial is adequate and moderately convincing
	Responses in T cell therapy	Evidence exists for the antigen as target of therapeutic response in T cell therapy
	Pre existent immunity correlates with survival	Pre existent B cell or T cell-mediated immunity to this antigen has shown a positive correlation with survival
	Efficacy in appropriate animal models	The antigen has shown efficacy in appropriate animal models
	No data available	No data available

CRITERIA Subcriteria	RATING SCALE	LEVEL OF EVIDENCE in descending order
FORMULATION (cell preparation, delivery vehicle, adjuvant, etc.)		
Scientific validity	Activity of the proposed formulation with this antigen demonstrated in clinical trials	Data for immunogenicity of specific formulation in human trials is superb as judged by an informed expert
		Data for immunogenicity of specific formulation in human trials is adequate
	Activity of the formulation class with this antigen demonstrated in clinical trials	Data for immunogenicity of the formulation class in human trials is superb as judged by an informed expert
		Data for immunogenicity of the formulation class in human trials is adequate
	Activity of the proposed formulation with this antigen demonstrated in animal models	Data in animal models for anti-tumor response of the specific formulation is superb as judged by an informed expert, spectacular potential for major effect in humans
		Data in animal models for immunogenicity or anti-tumor response of specific formulation is adequate
	Activity of the formulation class with this antigen demonstrated in animal models	Adequate data in animal models for the immunogenicity or anti-tumor efficacy of the formulation class
	No data available	No data available
Feasibility	Manufacturing of clinical grade formulation	GMP/clinical grade manufacturing of formulation at scale is reproducible and reliable
		Scalable clinical grade manufacturing process for the formulation has been piloted
	Manufacturing of clinical grade formulation for class-related agents	Scalable clinical grade manufacturing for the formulation class demonstrated
	Available as a laboratory formulation only	Laboratory formulation only
	Not formulated	Formulation not completely developed

CRITERIA Subcriteria	RATING SCALE	LEVEL OF EVIDENCE in descending order
IMMUNE MODIFIER AGENT (cytokines, etc.)		
Scientific validity	Augments specific immunity in human trials	Data for augmenting specific immunity in human trials is superb as judged by an informed expert
		Data for augmenting specific immunity in human trials is adequate
	Augments specific immunity in animals	Data for augmenting specific immunity in animals is superb as judged by an informed expert
		Data for augmenting specific immunity in animals is adequate
	Augments specific immune response in vitro	Adequate data for augmenting specific immunity in human cells in vitro
	No in vitro or in vivo data available	No in vitro or in vivo data available
Feasibility	Manufacturing of clinical grade agent	GMP/clinical grade manufacturing of the agent at scale is reproducible and reliable
		Scalable clinical grade manufacturing process for the agent has been piloted
	Manufacturing of clinical grade class-related modifier	Scalable clinical grade manufacturing process for the agent class has been demonstrated
	Available as a laboratory grade product	Laboratory product only
	Not developed	Not completely developed

CRITERIA Subcriteria	RATING SCALE	LEVEL OF EVIDENCE in descending order
COMBINATION REGIMEN		
Scientific validity	Activity of the specific combination demonstrated in human trials	Data available on immunogenicity of the specific combination in human trials
	Activity of combination of class-related molecules demonstrated in human trials	Data available on immunogenicity of combination for class-related molecules in human trials
	Activity of specific combination demonstrated in animal studies	Data available on anti-tumor response of specific combination in animal studies
	Activity of combination of class-related molecules demonstrated in animal studies	Data available on anti-tumor response of combination of class-related molecules in animal studies
	Theoretical basis exists for presumed efficacy of combination	Outstanding theory for efficacy of combination
		Adequate theory for efficacy of combination
		Weak rationale or rationale not adequately developed for combination

Feasibility	All products available for human use	All products are available for human use
	All products but one available for human use	All products are available except for one which can be manufactured for human use within the foreseeable future
	Products can be available for human use	More than one product is not available, but all can be manufactured for human use within the foreseeable future
	Products are laboratory formulations	Some products are available as laboratory formulations only
	Products are not available	No products likely to be available within foreseeable future (i.e., 2 years)

Supporting Tools Domain of the Immune Response Modifier Pathway

For additional information on biospecimen-based assays, please see the Biospecimen-Based Assessment Modalities Pathway (Clin Cancer Res 2008 14: 5672-5677).

For additional information on imaging-based assays, please see the Imaging-Based Assessment Modalities Pathway (Clin Cancer Res 2008 14: 5678-5684).

http://clincancerres.aacrjournals.org/content/vol14/issue18/#CCR_SPECIAL_FOCUS

CRITERIA Subcriteria	RATING SCALE	LEVEL OF EVIDENCE in descending order
ASSAY FOR IMMUNE RESPONSE		
Validity & Feasibility	Clinically validated assay to quantify immune response	Assay has been clinically validated (i.e., demonstrated to measure a clinically meaningful response)
	Assay to quantify immune response developed and standardized	Assay has been analytically validated (i.e., meets standards of accuracy and reproducibility)
	Assay to quantify immune response in development	Assay is developed but not standardized or validated
	Assay to quantify immune response not available	A suitable assay to quantify immune response needs to be developed
ASSAY TO SELECT PATIENT POPULATION		
Validity & Feasibility	Assay to select patient population validated in a prospective clinical study	Assay has been shown to successfully identify target patient population in a prospective clinical trial
	Assay to select patient population validated in a retrospective or integrated correlative study	Assay shows promise in identifying target patient population using large numbers of samples from an appropriate patient cohort or an integrated correlative study
	Assay to select patient population in development	Assay to select patient population has been developed and analytically validated/standardized
		Assay to select patient population has been developed but not standardized or validated
	Assay to select patient population not available	Assay to select patient population needs to be developed

Clinical Trials Domain of the Immune Response Modifier Pathway

CRITERIA Subcriteria	RATING SCALE	LEVEL OF EVIDENCE in descending order
AVAILABILITY OF PATIENTS FOR TRIALS		
Scientific Validity	Cancer type and stage of disease for clinical testing identified	Excellent data to support choice of population or patient subset for initial clinical trials with efficacy endpoints as judged by an informed expert
		Reasonable basis for choice of population or patient subset for initial clinical trials with efficacy endpoints
	Population not specified	Population is not specified
Feasibility	Availability of patients/individuals with required characteristics for clinical trials	Patients with appropriate stage of disease commonly are available and standard therapy is unlikely to preclude proposed experimental therapy
		Patients with appropriate stage of disease are not commonly available due to rarity of the stage or disease state, or competing protocols or confounding commonly used treatment regimens